Journal of Cardiology Cases 19 (2019) 165–168

Contents lists available at ScienceDirect

Journal of Cardiology Cases

journal homepage: www.elsevier.com/locate/jccase

Case Report

Effective steroid therapy in an elderly patient with cardiac sarcoidosis and severe left ventricular dysfunction

Kyoko Odawara (MD)[a], Takahiro Inoue (MD)[a,*], Yoshitaka Hirooka (MD, PhD, FJCC)[a,b]

[a] Department of Hypertension and Heart Failure Center, Takagi Hospital, Fukuoka, Japan
[b] Fukuoka International University of Health and Welfare, Fukuoka, Japan

ARTICLE INFO

Article history:
Received 26 June 2018
Received in revised form 21 December 2018
Accepted 29 December 2018

Keywords:
Cardiac sarcoidosis
Steroid therapy
Heart failure
Left ventricular dysfunction

ABSTRACT

A 75-year-old woman with no significant medical history was admitted to our hospital with congestive heart failure. Echocardiography revealed left ventricle (LV) systolic dysfunction [LV ejection fraction (LVEF) 18%] and diffuse LV hypokinesis mimicking dilated cardiomyopathy. Her brain natriuretic peptide (BNP) level was elevated (1214.3 pg/mL). Standard medications for heart failure failed to ameliorate her cardiac failure symptoms. Echocardiography on admission revealed thickening of the basal interventricular septum without morphological changes. Cardiac magnetic resonance imaging showed late enhancement in the epicardial side dominance of the LV at the late phase. Lysozyme and soluble interleukin 2 receptor levels were elevated. No abnormalities were found in the lungs, eyes, or skin, and she was diagnosed with cardiac sarcoidosis. At 23 days after beginning treatment, the patient received oral steroid therapy (prednisolone 30 mg/day) along with standard heart failure medications. The dose was tapered by 5 mg at 4-week intervals and then maintained at 10 mg per day. At 17 days after initiating steroid therapy, her BNP value decreased and remained at a low level. Echocardiography showed improvement of the LV dimensions and LVEF. In patients with severe LV dysfunction diagnosed with cardiac sarcoidosis, we propose that careful steroid therapy be considered, even for elderly patients.
<**Learning objective:** Although little is known about cardiac sarcoidosis, it should be considered even in elderly patients with refractory arrhythmias or intractable heart failure. Considering cardiac sarcoidosis as an etiology as well as early initiation of steroid therapy in patients exhibiting severe left ventricular dysfunction may be beneficial.>

Introduction

Sarcoidosis is a multi-system disease characterized by non-caseating granulomas in the involved organs. Little is known about the underlying mechanism. Cardiac involvement in patients with sarcoidosis is associated with a poor prognosis. Heart failure, fatal arrhythmia, and myocarditis are significant prognostic factors in such patients [1]. Left ventricular (LV) dysfunction in patients with cardiac sarcoidosis accompanied by active inflammation may rapidly progress over a short period [2]. Epidemiologic observations indicate that cardiac sarcoidosis can occur in elderly patients, particularly in women [3]. Appropriate therapies including steroids may prevent the progression, particularly in cases with active sarcoidosis-related inflammation. Early diagnosis and early treatment are critically important [4]. The present report describes a case of LV dysfunction with a diagnosis of cardiac sarcoidosis that was successfully treated with prompt steroid therapy.

Case report

A 75-year-old woman with no significant medical history was admitted to our hospital with congestive heart failure. She had dyspnea on effort. Upon arrival at our hospital, her blood pressure was 122/70 mmHg, her heart rate was 78 bpm, and she was New York Heart Association class II. An electrocardiogram (ECG) showed first-degree atrioventricular block and incomplete left bundle branch block (Fig. 1B). Echocardiography showed a LV ejection fraction (LVEF) of 18% and diffuse LV hypokinesis mimicking dilated cardiomyopathy. A chest X-ray showed cardi-

* Corresponding author at: Department of Hypertension and Heart Failure Center, Takagi Hospital, 141-11 Sakemi, Okawa City, Fukuoka, 831-0016, Japan.
E-mail address: ta-inoue@cardiol.med.kyushu-u.ac.jp (T. Inoue).

https://doi.org/10.1016/j.jccase.2018.12.019
1878-5409/

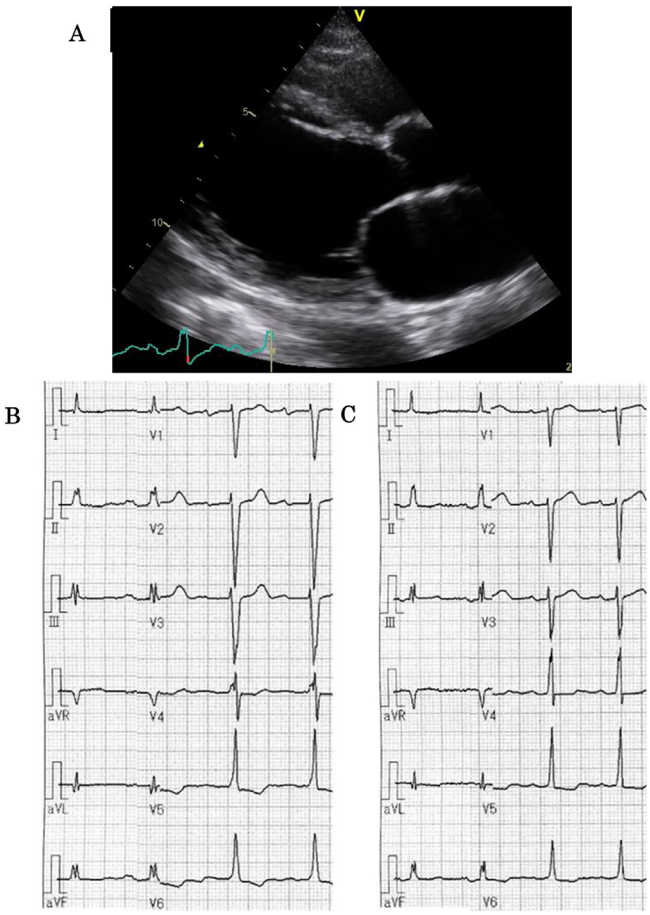


Fig. 1. The long-axial view of the echocardiogram showed thickening of the interventricular septum (5 mm) (A). The electrocardiogram (ECG) obtained on admission showed first-degree atrioventricular block with escape beats of the incomplete left bundle branch type (B). ECG after 6 months of oral steroid therapy showed almost normal sinus rhythm (C).

omegaly (cardiothoracic ratio 58%). Pleural effusion and bilateral hilar lymphadenopathy, however, were not seen. The patient's plasma brain natriuretic peptide (BNP) level was elevated (1214.3 pg/mL), but other laboratory data showed no markedly abnormal values. Standard medications for heart failure, including carvedilol 5 mg, enalapril maleate 2.5 mg, and furosemide 20 mg per day were started, but failed to ameliorate her cardiac failure symptoms. During 18 days of treatment, her body weight decreased from 45.7 to 43.7 kg, but her BNP level gradually increased from 1214 to 1533 pg/dl. Therefore, we reviewed the echocardiogram obtained on admission, and observed thickening of the basal interventricular septum (5 mm) without morphological changes (Fig. 1A). The basal interventricular septum became thinner and LV dilatation had advanced compared with findings in 2008.

Gadolinium-enhanced cardiovascular magnetic resonance imaging (MRI) was performed to evaluate for myocardial inflammation and revealed late enhancement in the epicardial side dominance of the LV at late phase (Fig. 2A). No abnormalities in sarcoidosis were found in the lung field.

It was thus necessary to distinguish sarcoidosis from myocarditis. Myocarditis could be ruled out, because markers of acute inflammation, such as a high number of white blood cells, C-reactive protein, creatine kinase, and troponin T, were not detected by laboratory blood tests. On the other hand, lysozyme and soluble interleukin 2 receptor levels were modestly elevated. Serum angiotensin-converting enzyme was not elevated. ^{67}Gallium imaging showed no abnormal findings, and the patient declined ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET). No abnormalities were detected in the eyes and skin. For the lungs, a chest X-ray has several limitations in detecting the pulmonary disease in sarcoidosis. For this reason, we undertook evaluation via a follow-up chest computed tomography scan two months after her hospitalization. There was no evidence to identify pulmonary sarcoidosis, such as bilateral hilar lymphadenopathy, diffuse ground glass opacities, and bilateral pleural effusions. She was therefore diagnosed with not systemic but presumptive isolated cardiac sarcoidosis based on the Japanese Diagnostic Criteria of Cardiac Sarcoidosis 2016 [5].

At 23 days after initiating treatment, the patient received oral steroid therapy (30 mg/day) along with the medications described above. The dose was tapered by 5 mg at 4-week intervals, and then maintained at 10 mg per day. Steroid therapy did not worsen the state of heart failure. Both the LVEF based on an echocardiography and serum BNP value gradually improved. At 17 days after initiating steroid therapy, her BNP value had decreased from 1533 to 418 pg/mL and remained at a low level. At 11 days after starting this strategy, echocardiography showed improvement of the LV dimensions and LVEF (Fig. 3). A chest X-ray showed a marked reduction in the cardiothoracic ratio (48%) without lung congestion. Because it would take more time to find the improvement of heart failure by the standard therapy only, its effectiveness is not excluded.

Six months later, steroid therapy (prednisolone 10 mg/day) continued. Repeated echocardiography showed improvement in

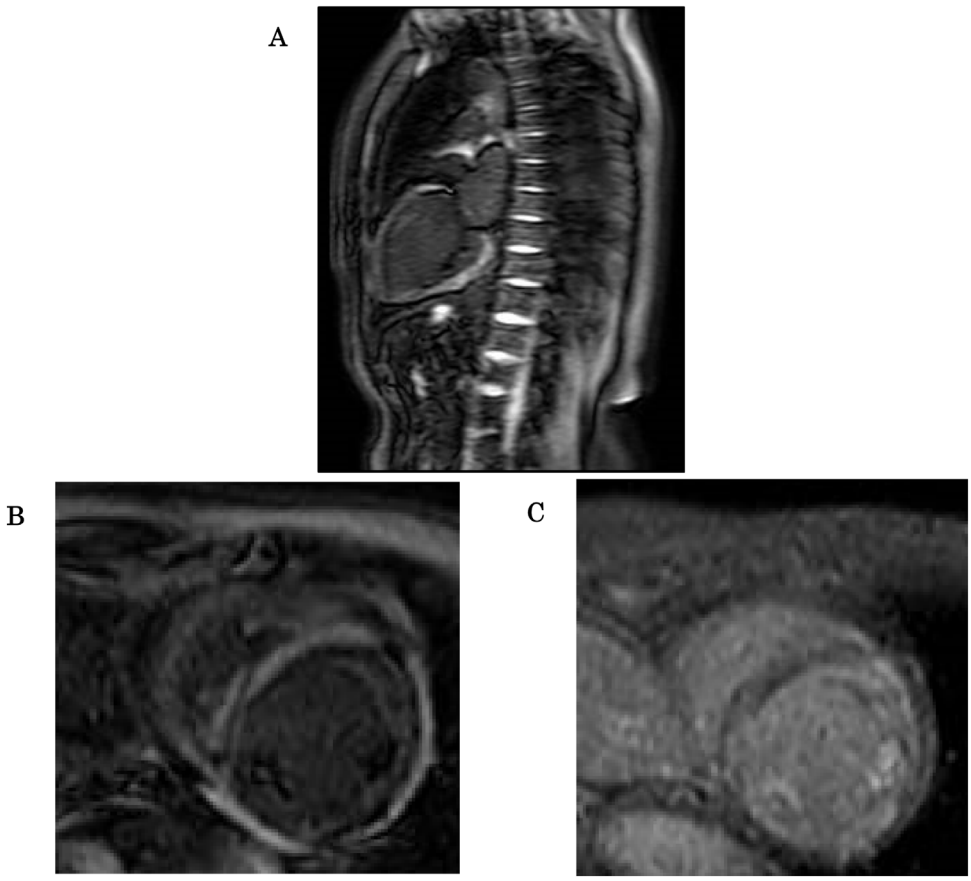


Fig. 2. Cardiac magnetic resonance imaging before steroid therapy showed hyperenhancement in the epicardial side dominance of the left ventricle, especially in the basal interventricular septum; (A) long-axis view; (B) short-axis view. Areas of hyperenhancement in the basal interventricular septum were considerably decreased after steroid therapy (C).

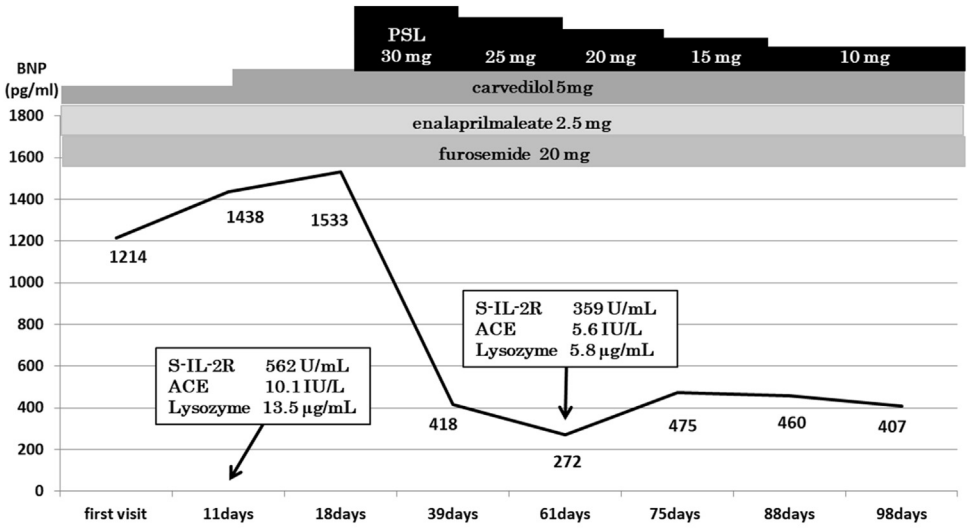
the LVEF. ECG revealed normal sinus rhythm (Fig. 1C). On MRI, the contrast-enhanced areas were considerably decreased (Fig. 2B, C). She had no heart failure symptoms and maintained independence in activities of daily living. Both the LV wall motion and serum BNP level gradually improved. In addition, the EF and E/e` were ameliorated due to decrease in both end diastolic volume and end systolic volume after starting steroid therapy.

Discussion

Cardiac sarcoidosis was first reported in 1929. The efficacy of steroid therapy has been increasingly controversial. In the 1970s, steroid therapy for patients with cardiac sarcoidosis was usually avoided because there was no objective evidence of benefit [6]. In the past few decades, however, steroids have become mandatory for cardiac sarcoidosis to resolve active myocardial inflammation. ^{67}Gallium imaging, ^{18}F-FDG PET, and MRI are used to evaluate the inflammation and the response to steroid treatment. Several studies revealed that patients with a preserved LVEF receiving steroid therapy have a good prognosis compared with untreated patients [7]. In general, initiation of steroid therapy may be therapeutic and effective for ameliorating LV remodeling and preserving LVEF in the early and middle stages of the disease, but may not be effective in the late stage [8]. The most unique aspect in the current case was that steroid therapy effectively ameliorated the decrease in LVEF, even though the patient had a very low LVEF, despite the absence of a sarcoidosis-related inflammatory response at diagnosis. We considered the crucial issue to be whether the resolution of inflammation was associated with an improvement in the LVEF. Takaya et al. showed that resolution of active myocardial inflammation by steroid treatment is not linked to a functional response to steroids, because if the myocardial tissue is inflamed, fibrotic, and scarred, then the functional response may be minimal [9]. According to Kandolin et al., LVEF is significantly improved in patients with severely impaired LVEF, but not in patients with normal or moderately depressed LVEF at the start of treatment [10]. Our finding may also support their description. More prospective studies are needed to determine the relationship among steroid therapy, sarcoid-related inflammation, and LVEF.

Only 40%–50% of patients with cardiac sarcoidosis diagnosed at autopsy were diagnosed during their lifetime. Novel diagnostic tools, however, such as MRI and PET imaging, may facilitate the diagnosis of cardiac sarcoidosis [11]. In particular, further evaluation is sometimes difficult in elderly patients with severe LV dysfunction in the absence of coronary artery disease, which does occur particularly in women [4].

In conclusion, we recommend a comprehensive effort to investigate the potential etiology of refractory arrhythmias and intractable heart failure, including cardiac sarcoidosis. Although detection of cardiac sarcoidosis at an early stage without LV dysfunction is preferable, prompt early initiation of steroid therapy, even in patients with severe LV dysfunction, should be considered. Moreover, steroid therapy may improve the clinical outcome, even in patients with no evidence of active cardiac inflammation on diagnostic imaging.



steroid therapy started at 23days

	first visit	19 days	34 days	56 days	85 days	103 days
LVDd (mm)	58	52	53	54	45	43
LVDs (mm)	53	48	45	46	38	37
LVEDV (ml)	100	102	88	98	50	57
LVESV (ml)	81	82	56	64	32	37
E/e'	54.67	43.52	17.5	17.64	22.14	17.33
LVEF (%)	18	20	36	35	36	36

Fig. 3. Changes in LV volume, LV function, and BNP level.
BNP: brain natriuretic peptide.
S-IL-2R: soluble interleukin-2 receptor.
ACE: angiotensin converting enzyme.
LVDd: left ventricular end-diastolic diameter.
LVDs: left ventricular end-systolic diameter.
LVEDV: left ventricular end-diastolic volume.
LVEF: left ventricular ejection fraction.

Conflict of interest

The authors declare that there is no conflict of interest.

References

[1] Iwaki K, Tachibana T, Takeumura T, Matsui Y, Kitaichi M, Kawabata Y. Pathological studies on sarcoidosis autopsy. I. epidemiological features of 320 cases in Japan. Acta Pathol Jpn 1993;43:372–6.
[2] Kakizaki R, Koitabashi T, Minami Y, Nabeta T, Kaida T, Ishii S, et al. Untreated cardiac sarcoidosis with active inflammation: severe left ventricular dysfunction and ventricular wall thinning in three years. J Cardiol Cases 2017;16:141–3.
[3] Sawahata M, Sugiyama Y, Nakamura Y, Nakayama M, Mato N, Yamasawa H, et al. Age-related and historical changes in the clinical characteristics of sarcoidosis in Japan. Respir Med 2015;109:272–8.
[4] Yazaki Y, Isobe M, Hiroe M, Morimoto S, Hiramatsu S, Nakano T, et al. Prognostic determinants of long-term survival in Japanese patients with cardiac sarcoidosis treated with prednisone. Am J Cardiol 2001;88:1006–10.
[5] The Japanese Circulation Society (JCS). Guidelines for the diagnosis and treatment of cardiac sarcoidosis (JCS2016) (Chair: fumio Terasaki);Published on February 24, [in Japanese]. 2017, http://www.j-circ.or.jp/guideline/pdf/JCS2016_terasaki_h.pdf.
[6] Scadding JG. The treatment of sarcoidosis. Prescribers J 1972;59:125.
[7] Chiu CZ, Nakatani S, Zhang G, Tachibana T, Ohmori F, Yamagishi M, et al. Prevention of left ventricular remodeling by long-term corticosteroid therapy in patients with cardiac sarcoidosis. Am J Cardiol 2005;95:143–6.
[8] Sadek MM, Yung D, Birnie DH, Beanlands RS, Nery PB. Corticosteroid therapy for cardiac sarcoidosis: a systematic review. Can J Cardiol 2013;29:1034–41.
[9] Takaya Y, Fukushima K, Nakamura K, Kaji M, Shinya T, Kanazawa S, et al. Reduction of myocardial inflammation with steroid is not necessarily associated with improvement in left ventricular function in patients with cardiac sarcoidosis: predictors of functional improvement. Int J Cardiol 2014;176:522–5.
[10] Kandolin R, Lehtonen J, Airaksinen J, Vihinen T, Miettinen H, Ylitalo K, et al. Cardiac sarcoidosis epidemiology, characteristics, and outcome over 25 years in a nationwide study. Circ J 2015;131:624–32.
[11] Birnie DH, Nery PB, Ha AC, Beanlands RSB. Cardiac sarcoidosis. J Am Coll Cardiol 2016;68:411–21.